IN THE CLAIMS:

Please amend claims 42 and 56-60, and cancel claims 1-41 and 55 as follows.

Claims 1-41 (canceled).

42. (currently amended) A null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation.

43. (previously presented) The null mutant mouse of claim 42, wherein functional PTTG protein is not expressed in the somatic cells of said mouse.

44. (previously presented) The null mutant mouse of claim 42, wherein the cells of said mouse lack the ability to endogenously express functional PTTG protein.

45. (previously presented) The null mutant mouse of claim 42, wherein both PTTG genes have been artificially mutated by way of homologous recombination.

46. (previously presented) The null mutant mouse of claim 42, wherein the PTTG null mutant was generated by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele.

47. (previously presented) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination.

48. (previously presented) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell.

49. (previously presented) The null mutant mouse of claim 48, wherein the embryonic stem cell is from the stem cell line murine ES J-1.

50. (previously presented) The null mutant mouse of claim 48, wherein said embryonic stem cell is injected into a blastocyst, and wherein the blastocyst is implanted into a pseudopregnant mouse.

51. (previously presented) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell, and wherein at least one mouse genomic copy of the PTTG gene in the embryonic stem cell recombines with a targeting vector containing a selectable genetic marker sequence, such that said targeting vector is inserted into the genome of said embryonic stem cell.

52. (previously presented) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele contains a deletion of the translation start site, the KOZAK region, a segment of the endogenous PTTG gene promoter region, the transcription start codon, or any combination thereof.

53. (previously presented) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of site specific recombination, transportational recombination, a frame shift mutation, homologous recombination in a germ cell, or any combination thereof.

54. (previously presented) The null mutant mouse of claim 53, wherein the germ cell is an oocyte or a male germ cell.

Claim 55 (canceled).

56. (currently amended) A mouse whose germ line comprises an artificially induced PTTG null mutation <u>on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature</u>

centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation, and wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG KOZAK sequence from which the KOZAK sequence has been deleted and replaced with polynucleotides exogenous to the PTTG gene, and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous KOZAK sequence.

57. (currently amended) A mouse whose germ line comprises an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation, and wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG translation start site from which the translation start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to

polynucleotide regions of an endogenous PTTG gene which flank the endogenous translation start site.

58. (currently amended) A mouse whose germ line comprises an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation, and wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG transcription start codon from which the transcription start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous transcription start codon.

59. (currently amended) An animal model for diabetes comprising a null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting diabetes, the prevalence of which is greater than in a mouse lacking said mutation.

60. (currently amended) A method for studying mammalian physiology at the cellular level, tissue level, organismal level or any combination thereof, comprising:

providing a null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation on both PTTG alleles, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia,

hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation; and

using the null mutant mouse in the study of mammalian physiology.

61. (previously presented) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of diabetes, hyperglycemia, hypoinsulinaemia, and hypoleptinemia.

62. (previously presented) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of chromosomal aneuploidy, premature centromere division, chromosomal damage, the mitotic cellular pathway, and cell cycle control.

63. (previously presented) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of thrombocytopenia, thymic hyperplasia, and splenic hypoplasia.

64. (previously presented) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of testicular hypoplasia and female subfertility.